Amendments

In the Claims:

Please cancel claim 1 without prejudice to or disclaimer of the subject matter recited therein.

Please add the following claims:

54. (New) A method for identifying a ligand that binds to a protein, comprising the steps of:

(1) receiving unfolding data that indicates thermal unfolding as a function of temperature for a protein incubated with a molecule tested for binding;

(2) determining an unfolding temperature midpoint for the protein in the presence of the molecule from the unfolding data;

(3) comparing the unfolding temperature midpoint for the protein incubated with the ligand with the unfolding temperature midpoint for the protein in the absence of any molecules tested for binding; and

(4) determining that the molecule tested for binding binds to the protein when a difference between the unfolding temperature midpoint for the protein in the presence of the molecule and unfolding temperature midpoint for the protein in the absence of any molecules tested for binding exceeds a threshold.

55. (New) The method according to claim 54, wherein step (2) comprises the step of plotting thermal unfolding as a function of temperature for the protein incubated with the molecule, and determining the unfolding temperature midpoint for the protein in the presence of the molecule from the plot.

56. (New) The method according to claim 55, further comprising the steps of:

(5) receiving data that indicates thermal unfolding as a function of temperature for the protein in the absence of any molecules tested for binding;

(6) plotting thermal unfolding as a function of temperature for the protein in the absence of any molecules tested for binding; and

(7) determining the unfolding temperature midpoint for the protein in the absence of any molecules tested for binding from the associated plot.

57. (New) The method according to claim 54, wherein the molecule that binds is a ligand, and further comprising the step of:

(5) estimating ligand binding affinity.

58. (New) The method according to claim 57, wherein step (5) comprises the step of estimating the ligand binding affinity at the unfolding temperature midpoint.

59. (New) The method according to claim 58, wherein step (5) comprises the step of estimating the ligand binding affinity at the unfolding temperature midpoint according to:

$$K_L^{T_m} = \frac{\exp\left\{-\frac{\Delta H_u^{T_0}}{R}\left[\frac{1}{T_m}-\frac{1}{T_0}\right]+\frac{\Delta C_{pu}}{R}\left[\ln\left(\frac{T_m}{T_0}\right)+\frac{T_0}{T_m}-1\right]\right\}}{\left[L_{T_m}\right]}$$

where,

$K_L^{T_m}$ is a ligand association constant at T_m;

T_m is a midpoint temperature for the protein unfolding transition in the presence of the ligand;

T_0 is a midpoint temperature for the protein unfolding transition in the absence of the ligand;

$\Delta H_u^{T_0}$ is an enthalpy of protein unfolding in the absence of ligand at T_0;

ΔC_{pu} is a change in heat capacity upon protein unfolding in the absence of ligand;

$\left[L_{T_m}\right]$ is a free ligand concentration at T_m ; and

R is the gas constant.

60. (New) The method according to claim 59, further comprising the step of:

(6) inserting actual values $\Delta H_u^{T_0}$ and ΔC_{pu} into the equation of step (5).

61. (New) The method according to claim 59, further comprising the step of:

(6) estimating values for $\Delta H_u^{T_0}$ and ΔC_{pu} for use in the equation of step (5).

62. (New) The method according to claim 61, wherein step (6) comprises the steps of:

(a) fitting the data with a least squares algorithm according to:

$$y(T) = y_u + \frac{(y_f - y_u)}{1 + \exp\left[\left[\frac{-\Delta H_u}{R}\right]\left[\frac{1}{T} - \frac{1}{T_m}\right] + \left[\frac{\Delta C_{pu}}{R}\right]\left[\left(\frac{T_m}{T} - 1\right) + \ln\frac{T}{T_m}\right]\right]}$$

where,

$y(T)$ is fluorescence unfolding data as a function of temperature T;

y_u is a pre-transitional fluorescence intensity,

y_f is a post-transitional fluorescence intensity;

ΔH_u is a protein unfolding enthalpy;

ΔC_{pu} is a change in heat capacity upon protein unfolding;

T_m is a midpoint temperature for protein unfolding transition in the presence of the ligand;

(b) varying values for y_u, y_f, ΔH_u, ΔC_{pu}, and ΔC_{pu} until a suitable curve fit is obtained; and

(c) using resultant values from step 9(b) in step (5).

63. (New) The method according to claim 59, further comprising the step of:

(6) determining a ligand binding constant, for any temperature T, according to:

$$K_L^T = K_L^{T_m} \exp\left\{ -\frac{\Delta H_L^T}{R}\left[\frac{1}{T} - \frac{1}{T_m}\right] + \frac{\Delta C_{pL}}{R}\left[\ln\left(\frac{T}{T_m}\right) - \frac{T}{T_m} + 1\right]\right\}.$$

64. (New) The method according to claim 58, further comprising the step of:

(6) determining a ligand binding constant, for any temperature T, according to:

$$K_L^T = K_L^{T_m} \exp\left\{ -\frac{\Delta H_L^T}{R}\left[\frac{1}{T} - \frac{1}{T_m}\right]\right\}.$$

65. (New) The method according to claim 54, wherein step (1) comprises the step of receiving fluorescence data.

66. (New) The method according to claim 63, wherein step (1) further comprises the step of plotting thermal unfolding according to a non-linear, least squares fitting algorithm.

67. (New) A computer program product comprising a computer useable medium having control logic embodied in said medium, for causing a computer to process thermal unfolding data, said control logic comprising;

a thermal unfolding data generating routine that causes the computer system to generate thermal unfolding data from fluorescence information received from a plurality of samples;

a thermal unfolding curve generation routine that causes the computer system to generate thermal curves from the thermal unfolding data; and

a thermal unfolding curve comparison routine that causes the computer system to compare the thermal unfolding curves.

68. (New) A computer program product comprising a computer useable medium having control logic embodied in said medium, for causing a computer to process thermal unfolding data, said control logic comprising:

a thermal unfolding data generating routine that causes the computer system to generate thermal unfolding data from fluorescence information received from a plurality of samples;

a thermal midpoint determining routine that causes the computer system to determine thermal unfolding midpoint temperatures from the thermal unfolding data; and

a thermal midpoint comparison routine that causes the computer system to compare the thermal unfolding midpoint temperatures.

69. (New) The computer program product according to claim 68, wherein said thermal midpoint determining routine comprises a thermal unfolding curve generation routine that causes the computer system to generate thermal curves from the thermal unfolding data and to determine the thermal unfolding temperature midpoints from the curves.

70. (New) The computer program product according to claim 68, wherein said control logic further comprises:

a positioning control routine that causes the computer system to control a positioning system for the plurality of samples.